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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/633,141	08/01/2003	Lynn Allen-Hoffmann	STRATA-08318	3101

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MEDLEN & CARROLL, LLP
101 HOWARD STREET
SUITE 350
SAN FRANCISCO, CA 94105

EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/633,141	ALLEN-HOFFMANN ET AL.	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17 and 27-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17 and 27-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *0806*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-17 and 27-38 in the reply filed on July 31, 2006 is acknowledged. It is noted that non-elected claims 18-26 have been canceled, such that claims 1-17 and 27-38 are pending and under consideration.

2. Applicant's election of SEQ ID NOS 1 and 3 in the reply filed on November 24, 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Applicant's identification of claims readable upon SEQ ID Nos 1 and 3 in the reply of March 27, 2007 is also acknowledged. It is noted that although the Election/Restriction of June 30, 2006 required an election of only a single probe of those set forth in claims 10 and 27, both SEQ ID NOS 1 and 2 have been addressed herein, as search and examination of these 2 particular sequences together did not prove unduly burdensome. Further, methods employing SEQ ID NOS 3 and 4 have been searched and examined.

Information Disclosure Statement

3. With regard to the US patent document identified by citation number 19 on the IDS filed July 31, 2006, it is noted that the listed patent number corresponds to a document that is not available as the patent has been withdrawn. Accordingly, this document could not be considered by the examiner.

Specification

4. The disclosure is objected to because of the following informalities: in the amendment of April 9, 2004, applicant directed the entry of the sequence listing at the wrong location in the specification (specifically, the correct order is: claims, abstract, sequence listing; not: sequence listing, claims, abstract).

Appropriate correction is required.

Oath/Declaration

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because it includes a claim for benefit of a provisional application under 35 USC 120, when such a claim must be made under 35 USC 119(e).

Claim Rejections - 35 USC § 112, first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-17 and 27-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods employing cell samples and/or nucleic acids obtained therefrom, does not reasonably provide enablement for methods employing any "cell product derived from" a cell sample. The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims are drawn to methods for detecting species-specific nucleic acid in which detection is accomplished via exposure of a sample to nucleic acid probes under hybridization conditions. The claims state that the sample is "selected from the group consisting of a first cell sample from a first species and a cell product derived from said first cell sample" (see independent claims 1 and 27, step a)i)). The specification does not include any kind of limiting definition of the term "cell product," and it is well known to those of skill in the art that numerous types of products may be derived from cells, including not only nucleic acids, but a vast array of other materials (e.g., proteins, lipids, fats, components thereof, etc.). The specification provides teachings with regard to hybridization of nucleic acid probes to target nucleic acid molecules, and exemplifies the detection of target sequences in genomic nucleic acids isolated from such samples as

cells and biopsies (see Examples 1-7). However, the specification is silent with regard to the use of any type of "cell product" other than nucleic acids. Absent guidance from the specification, one of skill in the art may look to the teachings of the prior art for further guidance and enablement of a claimed invention. However, in the instant case, the prior art is silent with regard to methods of nucleic acid detection via hybridization to cell products that do not in fact contain nucleic acid. One of skill in the art would have no expectation that even an infinite quantity of experimentation would allow for the detection of species-specific nucleic acid in any kind of "cell product" that lacks nucleic acid. Thus, as the claims as presently written encompass methods in which species-specific nucleic acids are to be detected in any type of "cell product" including numerous types of cell products that would not include any kind of target for detection, it would clearly require undue experimentation to use applicant's invention in a manner reasonably commensurate with the instant claims.

Claim Rejections - 35 USC § 112, second paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-17 and 27-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-17 are indefinite because it is unclear whether the claims are drawn to a method for "detecting species-specific nucleic acid," as set forth in the preamble of claim 1, or to methods of exposing a sample to probes to "facilitate the detection" of

nucleic acids. In particular, while the preamble of the claim appears to require detection of "species-specific nucleic acid," the actual method steps set forth in the claims do not appear to actually require such detection. Clarification is required.

Claim 3 is indefinite over the recitation "wherein said repetitive element is present in at least 20 copies" because it is not clear how this recitation further limits the claimed method. In particular, this language does not make clear where the repetitive element must be present "in at least 20 copies" (e.g., does this requirement pertain to the sample being examined, the genome of the "second species," etc.).

Claim 5 is indefinite over the recitation of the limitation "said second cell sample" because there is insufficient antecedent basis for this limitation in the claims.

Claims 13-14 are indefinite over the recitation of the limitation "said cultured human skin tissue" in claim 13 because there is insufficient antecedent basis for this limitation in the claims. It appears that claim 13 was intended to depend from claim 12 (rather than claim 11).

Claims 16-17 are indefinite over the recitation of the limitation "said second cell sample" in claim 16 because there is insufficient antecedent basis for this limitation in the claims.

Claims 27-38 are indefinite because it is unclear whether the claims are drawn to a method for "detecting species-specific nucleic acid," as set forth in the preamble of claim 27, or to methods of exposing a sample to probes to "facilitate the detection" of nucleic acids. In particular, while the preamble of the claim appears to require detection

of "species-specific nucleic acid," the actual method steps set forth in the claims do not appear to actually require such detection. Clarification is required.

Claim 29 is indefinite over the recitation "wherein said repetitive element is present in at least 20 copies" because it is not clear how this recitation further limits the claimed method. In particular, this language does not make clear where the repetitive element must be present "in at least 20 copies" (e.g., does this requirement pertain to the sample being examined, the genome of the "second species," etc.).

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1, 4-8, and 15-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al (US 6,924,141 B2 [8/2/05; filed 3/30/01]).

It is noted that the subject matter relied upon in the instant rejection finds support in provisional application 60/193,771 (filed March 31, 2000), of which the '141 patent claims the benefit.

Morgan et al teach methods in which mouse dermal papilla (DP) cells are co-cultured with chicken embryo fibroblasts (CEFs) infected with a retroviral vector encoding chick Shh (see entire reference, particularly col 15, line 11-col 18, line 17). Morgan et al disclose analyzing DP cells for expression of Shh and 3 other genes (ptc-1, gli-1, and beta-actin) "immediately after isolation and after three passages in culture" alone (see col 17, lines 25-28). Morgan et al also disclose analyzing DP cells for expression of ptc-1, gli-1 and beta actin by PCR using mouse-specific primers following co-culture with the Shh-expressing CEFs (see col 17, lines 49-60), stating that "murine specific primers were employed to discriminate between gene expression in the DP and feeder cell populations" (col 17, lines 58-60). Morgan et al further teach the subsequent grafting of the DP cells previously co-cultured with Shh-expressing CEFs on the backs of nude mice to determine whether the co-culture process leads to hair growth (see col 17, line 60-col 18, line 7). Morgan et al do not teach testing of the DP cell-population for the presence of chick Shh sequences prior to grafting. However, in view of the teachings of Morgan et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have conducted such testing. As noted above, Morgan et al discloses testing for Shh expression in DP cells prior to co-culture, and the purpose of Morgan et al's assays are to determine the effects of an exogenous source of Shh on gene expression and hair growth in the DP cells. Thus, an

ordinary artisan would have been motivated to have tested the DP cells for Shh prior to grafting for the advantages of confirming the absence of feeder cells in the pool of cells to be grafted, and/or to confirm that Shh expression was still lacking in the DP cells.

With further regard to claim 4, the mouse cells of Morgan et al constitute a non-human cell sample. Regarding claim 5, it is noted that claim 1 never refers to a "second cell sample;" the only "cell sample" mentioned in claim 1 is a "first cell sample," and Morgan et al teach a mouse cell sample. Regarding claims 6-8, Morgan et al disclose the use of PCR in detection of target sequences, and (as noted above) disclose detection (by PCR) of multiple target sequences specific to the mouse DP cells. Regarding claim 15, as Morgan et al disclose that any cell type may be used in their methods (see, e.g., col 7, lines 24-31), it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Morgan et al so as to have employed therein any cell type of interest to a practitioner, including stem cells. Regarding claim 16, it is again noted that Morgan et al disclose co-culture in the presence of CEF feeder cells.

13. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al as applied to claims 1, 4-8, and 15-16, above, and further in view of Edwards et al (PCR Methods and Applications 3:65-75 [1994]).

The teachings of Morgan et al are set forth above. While Morgan et al teaches and suggests PCR of multiple target sequences in both DP cells and feeder cells, as set forth above, Morgan et al does not teach multiplex PCR, as required by the claim. Edwards et al teach that multiplex PCR has many advantages over conventional PCR,

including superior monitoring of PCR failure, template quality and quantity, and artifacts, and greater efficiency (see entire reference, particularly pages 565-566). Accordingly, in view of the teachings of Edwards et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the PCR detection of Morgan et al so as to have practiced it in a multiplex fashion in order to have achieved any or all of the benefits taught by Edwards et al.

14. Claims 12-14 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al as applied to claims 1, 4-8, and 15-16, above, and further in view of Allen-Hoffmann et al (J. Invest. Dermatol. 114(3):444-455 [2000])(cited in the IDS of 7/31/06).

Regarding claims 13-14, it is noted that while the claims depend from claim 11, it appears that the claims were intended to depend from claim 12, as they are further limiting of "said cultured human skin tissue." This rejection applies to the claims to the extent that they were intended to depend from claim 12.

The teachings of Morgan et al are set forth above. It is again noted that Morgan et al disclose that any cell type may be used in their methods (see, e.g., col 7, lines 24-31). Morgan et al also explicitly teach the use of human cells (see, e.g., col 9, lines 29-31), and it is noted that the preferred cell type employed by Morgan et al (the DP cells) are epithelial cells. However, Morgan et al do not teach the use in their methods of NIKS cells or any other cultured human skin tissue. Allen-Hoffmann et al disclose a spontaneously immortalized human keratinocyte cell line termed "NIKS," and teach that NIKS cells are "an important new model for the study of human epidermal biology" (see

entire reference, particularly page 454). In view of the teachings of Allen-Hoffmann et al, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods of Morgan et al so as to have practiced them with NIKS cells in lieu of DP cells. An ordinary artisan would have been motivated to have made such a modification for the advantage of observing the effects of, e.g., Shh expression in a human cell model. Further, regarding claim 17, an ordinary artisan would have been motivated to have employed the same type of feeder cells taught by Allen-Hoffmann et al (specifically, mouse fibroblasts; see, e.g., p. 445, left column), rather than, e.g., experimenting to identify an appropriate type of feeder cell for NIKS cells, for the advantages of convenience and efficiency.

15. Claims 2-3, 10, 27-34, and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al in view of Allen-Hoffmann et al as applied to claims 12-14 and 17, above, and further in view of Boyle et al (Genomics 12(3):517-525 [1992]).

The teachings of Morgan et al and Allen-Hoffmann et al are set forth above. While the teachings of Morgan et al and Allen-Hoffmann et al suggest the use of NIKS cells and mouse fibroblast feeder cells, the references do not teach an appropriate mouse-specific target for analysis and identification of, e.g., contaminating mouse cells in a sample of cells isolated following co-culture. Boyle et al teach a large mouse-specific repeat sequence present in approximately 60-80 copies on mouse chromosome 8 (see entire reference). Boyle et al specifically teach that this repeat is absent in humans (see, e.g., the abstract). In view of the teachings of Boyle et al, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was

made to have employed the repeat sequence of Boyle et al as a target sequence for mouse cells when practicing the method suggested by Morgan et al and Allen-Hoffmann et al. An ordinary artisan would have been motivated to have employed such a target sequence because the sequence has been established by Boyle et al as being mouse specific and absent in human cells. Further, it is noted that sequences identical to SEQ ID NO 1 and to the reverse complement of SEQ ID NO: 2 flank the sequence taught by Boyle et al (see bracketed sequences in Figure 3). As primers targeting the 5' and 3' termini of a target sequence of interest are routinely selected for use in PCR, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have selected these particular sequences as primers so as to have successfully amplified the entire target sequence taught by Boyle et al.

16. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Morgan et al in view of Allen-Hoffmann et al and Boyle et al as applied to claims 2-3, 10, 27-34, and 37-38, above, and further in view of Edwards et al,

The teachings of Morgan et al, Allen-Hoffmann et al and Boyle et al are set forth above. While Morgan et al teaches and suggests PCR of multiple target sequences in both DP cells and feeder cells, the Morgan et al, Allen-Hoffmann et al and Boyle et al references do not teach multiplex PCR, as required by the claim. Edwards et al teach that multiplex PCR has many advantages over conventional PCR, including superior monitoring of PCR failure, template quality and quantity, and artifacts, and greater efficiency (see entire reference, particularly pages 565-566). Accordingly, in view of the teachings of Edwards et al, it would have been *prima facie* obvious to one of ordinary

skill in the art at the time the invention was made to have modified the PCR detection suggested by Morgan et al in view of Allen-Hoffmann et al and Boyle et al so as to have practiced it in a multiplex fashion in order to have achieved any or all of the benefits taught by Edwards et al.

Conclusion

17. It is noted that the prior art does not teach or suggest the use of a primer or probe consisting of SEQ ID NO: 3 and/or a primer or probe consisting of SEQ ID NO: 4 in the methods of the instant claims.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday and Thursday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571/272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Diana B. Johannsen
Primary Examiner
Art Unit 1634